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Relationship between Alcohol Use/Abuse, HIV Infection and Neuropsychological Performance in African American Men

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Abstract

This study examines the impact of alcohol use and HIV infection on neuropsychological performance in a sample of 497 community-resident African American men. HIV serostatus and alcohol use (during the past 12 months) exerted an interactive effect on psychomotor speed, reaction time, and motor speed, and in general, HIV infected heavy drinkers evidenced significantly poorer performance than other HIV positive subjects. Main effects for HIV serostatus were noted for reaction time, with seronegative men performing better than seropositives. This study examines a sample of men who continue to show increases in HIV infection, however, sample specific issues such as comorbid substance use, past histories of head injury, and lack of data on alcohol abuse and dependence require caution in definitively attributing the findings solely to alcohol and HIV. However, these findings suggest that relatively recent heavy alcohol use may represent a potential risk factor for more rapid or pronounced cognitive decline in HIV positive individuals, and that these patterns may be even more pronounced in persons with comorbid substance use.

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Numerous studies to date have investigated the synergistic effects of psychoactive drugs and HIV on disease progression and neuropsychological (NP) functioning (Bornstein et al., 1993; Concha et al., 1992; Durvasula et al., 2000; Marder et al., 1992; Selnes et al., 1997). These studies, which have largely examined the independent and interactive effects of heroin and cocaine abuse on NP functioning, have yielded mixed results, and most of these studies have been conducted with injection drug users. No studies have demonstrated any interactive effects between drug use and HIV on NP performance. Some studies have reported no differences between asymptomatic injection drug users and seronegative controls (Concha et al., 1992; Selnes et al., 1992). Bornstein et al. (1993) noted that neither recency nor severity of drug/alcohol abuse/dependence were associated with NP impairment in HIV infection —

however, the drugs of abuse were not clearly specified in their study. To date, few studies have focused on whether HIV and alcohol consumption operate synergistically to produce more marked cognitive impairment in HIV infected samples. This is a noteworthy oversight given the relatively high rates of alcohol abuse and dependence among HIV positive individuals (Boscarino, Avins, Woods, Lindan, Hudes, & Clark, 1995).

Alcohol Use and NP Performance

The adverse neuropsychological consequences of alcohol abuse and dependence are well documented. Mild to moderate NP deficits have been observed in individuals with histories of alcohol dependence (Oscar-Berman, Shagrin, Evert, & Epstein, 1997; Parsons & Nixon, 1993). Deficits are typically observed in attention, visuospatial functioning, executive functioning, and in learning and memory (Parsons & Nixon, 1993; Rourke & Loberg, 1996). There is a wide spectrum of effects as a function of alcohol abuse, with effects on memory ranging from temporary short-term memory deficits in social drinkers, to an anterograde amnesic syndrome in chronic alcohol abusers (Wilkinson & Poulos, 1987). There is also electrophysiological evidence of working memory deficits in alcohol abusers. Using event-related potential (ERP) technique, researchers have found that alcoholics make more errors and have longer response times compared to controls (Zhang, Begleiter, Porjesz, & Litke, 1997a).

Studies that have examined the combined abuse of alcohol and drugs on cognitive functioning have yielded mixed results. In general, and particularly in HIV infected cohorts, alcohol and drug use are commonly confounded, making it difficult to definitely draw conclusions about the contribution of either in isolation. In a study comparing the performance of alcoholics and polysubstance abusers, Bondi, Drake, and Grant (1998) found that cocaine abusers with concurrent alcohol abuse performed more poorly on measures of learning and recall relative to alcoholics without concomitant cocaine abuse. Beatty, Blanco, Hames, & Nixon (1997) examined spatial cognition in alcohol abusers both with and without concurrent abuse of other substances, and found that both polysubstance abusers (alcohol plus drugs) and alcohol abusers evidenced deficits in visuospatial perception, construction, and learning and memory. These results suggest that drug abuse may not confer additional risk for NP dysfunction above and beyond that attributable to alcohol abuse or may do so only in a subset of heavy drinkers. (Bates & Convit, 1999).

Neuroanatomical regions believed to be responsible for neuropsychological deficits in alcoholics include the cerebellum, frontal and limbic regions, and the basal forebrain (Parsons & Leber, 1982). Compared with nonalcoholic controls, alcoholics have shown significant reductions in cerebral blood flow in frontal areas; greater blood flow reduction in frontal cortical areas has been associated with greater severity of alcoholism and poorer NP functioning. (for review see Oscar-Berman & Hutner, 1993).

The mechanism by which alcohol use may impact HIV related disease progression is unclear. Alcohol abuse may lead to increased systemic immune dysfunction in HIV seropositive individuals via immune suppression (Bagasra, Whittle, Kajadacsy-Bafla, & Lischner, 1990). Wang and Watson (1995) reviewed animal and human studies and concluded that alcohol can serve as a cofactor in the development of AIDS in animals. However, in humans, these findings are not conclusive. Gentry (1998) observed similar immunological deficits when comparing pneumococcal disease in alcoholism and HIV infection, suggesting that these deficits may be exacerbated when HIV infection and alcohol abuse co-occur. Therefore, HIV seropositives who are co-morbid for alcohol abuse may be more vulnerable to HIV-related NP deficits than non-alcohol abusing seropositive individuals.

A few studies have investigated the impact of alcohol use and HIV on NP function. Fein, Biggins, and MacKay (1995) investigated the effect of chronic alcohol abuse and HIV infection on the frontal cortex, using the auditory P3A evoked potential. They found that HIV infection and active chronic alcohol abuse resulted in a lengthening of the P3A latency in a novel nontarget condition and that alcohol abuse worsened the P3A latency effect of HIV disease. The results demonstrated that alcohol abuse has deleterious effects on the functioning of the frontal cortex. In another study, auditory and spatial P3A latency increased with progression of HIV-associated cognitive impairments in the auditory and spatial modalities, respectively, and P3A latency indicated additive effects of the comorbidity of alcohol abuse and HIV infection (Fein, Fletcher, & Di Sclafani, 1998). In HIV seropositive light/nondrinkers, P3A latency delays occurred primarily in subjects with more advanced disease, whereas in HIV seropositive chronic heavy drinkers, P3A latency delays occurred even in asymptomatic seropositive subjects. Finally, Meyerhoff et al. (1995) described the effects of HIV and chronic alcohol abuse on brain phosphorous metabolites, and reported cumulative decreases in white matter concentrations of phosphodiester and phosphocreatine with HIV+ alcoholics compared to HIV+ light/nondrinkers and HIV- individuals. In addition, they described relatively lower concentrations of gray matter phosphodiester in alcoholics with AIDS compared to HIV-nondrinkers. In summary, these findings illustrate the additive effects of HIV and alcohol on electrophysiological and metabolic measures of CNS function. Quantitative indices of alcohol use, but not alcohol abuse or dependence have been found to be associated with NP performance in HIV infected individuals (Bornstein et al., 1993). Green, Saveanu, & Bornstein (2004) examined alcohol abuse and HIV and found that HIV and alcohol abuse history had interactive effects on verbal reasoning, auditory processing, and reaction time.

Other studies have failed to find evidence that chronic drinking influences the rate and progression of HIV infection (Dingle & Oei, 1997; Penkower et al., 1995) or NP functioning in HIV-infected individuals (Bornstein et al., 1993). Penkower et al. (1995) investigated patterns of change in alcohol consumption as well as frequency and amount of alcohol consumption in HIV seropositive men followed for approximately 6 years. Level of drinking at study entry was not associated with CD4+ cell counts and/or the development of AIDS-related symptoms at the final study visit. They suggested that the immunosuppressive effects of alcohol use may be overwhelmed by the immunosuppressive effects of the HIV-initiated cascade.

HIV and NP Performance

The deleterious effects of HIV infection on cognition are well established (Brew, Rosenblum, & Price, 1988; Ho et al., 1985; Levy, Shimabukuro, Hollander, Mills, & Kaminsky, 1986; Navia, Cho, Petito, & Price, 1986). Progressive decline in neuropsychological functioning is observed in a relatively large proportion of individuals, with 20–30% of patients with AIDS developing dementia before death (McArthur, 1994). NP dysfunction in HIV seropositive individuals is characterized by slowed performance on speeded tests, particularly tests with a psychomotor or motor component, attentional deficits, and memory impairment (Grant et al., 1987; Heaton et al., 1995; Miller et al., 1990). Language, visuospatial, and global cognitive functioning are typically intact in the early phases of HIV-associated CNS dysfunction, with substantial deficits in these domains observed only in late stage illness (van Gorp, Lamb & Schmitt, 1993).

The present study investigates the effects of alcohol use and HIV in a community sample of 497 African American men who differ on serostatus and alcohol use/abuse. Study of the effects of alcohol use and HIV infection among African American men is indicated given (a) the disproportionate rates of infection in this group, (b) the relative dearth of empirical data about the NP sequelae of HIV infection in African Americans; and (c) the absence of large scale

studies examining the interactive effects of alcohol and HIV on cognition. Rates of infection in African Americans are higher than for any other ethnic group, with African Americans accounting for nearly 50% of new AIDS cases during the past 6 years (Centers for Disease Control and Prevention, 2001). Based on recent findings highlighting the interactive effects of alcohol abuse and HIV on NP performance (Green et al., 2004), and given the current evidence on the NP sequelae of HIV infection and alcohol use, the following hypotheses were tested: (a) HIV positive men will evidence poorer NP performance than HIV negative men in those NP domains known to be affected by HIV (e.g., psychomotor and motor speed, memory, executive functioning); (b) “Heavy” drinkers (21 drinks or greater per week) will evidence poorer NP performance than light, moderate, and nondrinkers in those NP domains known to be affected by alcohol use (e.g., memory, psychomotor speed, executive functioning, visuospatial function); and (c) alcohol use and HIV serostatus will interact such that HIV positive individuals classified as heavy drinkers will evidence significantly poorer NP performance than seronegative heavy drinkers and seropositives with lower levels of alcohol consumption. These effects should be most evident in those domains most adversely affected by both alcohol use and HIV (e.g., memory, psychomotor speed, executive function).

Method

U.S.-born African American men between 18–50 years of age were recruited from Los Angeles County to participate in the African American Health Project (AAHP) (Myers et al., 1997). The AAHP was a NIDA-funded, multidisciplinary, cross-sectional study that examined medical, psychiatric, neurological, neuropsychological, and psychosocial aspects of HIV/AIDS and substance use/abuse in a community sample of English-speaking African American men. Data collection was conducted from 1992–1994. All testing was conducted in English. All men in the sample described their race/ethnicity as “Black.” In order to minimize potential confounding, men with low educational attainment or functional illiteracy ($\leq$ 8th grade education and/or impaired reading or comprehension), with non-HIV-related physical or sensory difficulties, or with acute medical, neurological or psychiatric conditions that might interfere with their ability to tolerate the intensive evaluation were excluded (e.g., current psychotic disorder and attendant functional impairment). All participants were screened by clinically trained interviewers (i.e., clinical psychologists, clinical psychology graduate students or by psychiatric residents).

In order to ensure a sample that was generally representative of the community of interest, men were not excluded if they had a history of head injury or loss of consciousness. In order to encourage participation, all participants were compensated for their time and provided with transportation and refreshments. No participants were tested if they appeared to be acutely intoxicated. Subject recruitment is described at length in Myers et al. (1997).

The sample was comprised of 497 men, including 310 HIV seronegatives and 187 HIV seropositives. Within the HIV+ sample, 77 were asymptomatic and 110 were symptomatic. HIV+ individuals were classified as asymptomatic versus symptomatic on the basis of 1987 CDC Staging Criteria (CDC, 2001), and WHO Staging Criteria. On this basis, individuals with CD4 counts below 200 were not classified as symptomatic in the absence of symptoms (a departure from the 1993 CDC Staging Criteria). Approximately half of the symptomatic seropositive individuals met criteria for AIDS as defined by the onset of secondary infectious disease, secondary cancers, or other AIDS defining conditions. The sample was also stratified on pattern of alcohol use in the past 12 months as follows: nondrinker (no alcohol consumption during the past year) ($N = 144$), light drinker (less than 7 drinks per week on average) ($N = 193$), moderate drinker (7–21 drinks per week on average) ($N = 80$), and heavy drinker (greater than 21 drinks per week on average) ($N = 80$). The cutoff for heavy drinking is similar to that

employed by other authors (e.g., Cook, Sereika, Hunt, Woodward, Erlen, & Conigliaro, 2001). See Table 1 for sample breakdown by HIV serostatus and alcohol use.

Mean age for the sample was 34.3 years ($SD = 7.8$), and mean educational level was 13.7 years ($SD = 2.2$). Fifty percent of the sample earned \$7,500 or less per year, and 67% of the sample was unemployed. Fifty percent of participants were categorized as men who have sex with men (MSM) or with men and women (MSMW) (92.5% of HIV+ participants were categorized as MSM/MSMW, and 25% of HIV- participants were categorized as MSM/MSMW).

Measures & Procedures

All participants completed comprehensive assessments conducted by a team of trained interviewers and examiners. The assessment battery included demographic information, medical history, measures of psychiatric history and status, neurologic and neuropsychological examinations, detailed description of past and current sexual practices, and measures of a range of psychosocial factors that could mediate the effects of substance use and HIV/AIDS. Blood and urine samples were obtained and tested for comprehensive serology, HIV, and toxicology testing by technicians who were blind to serostatus and substance use histories. Specifically, qualitative urine toxicology (Roche Abuscreen) was used in conjunction with standard laboratory toxicology to test for the presence of amphetamines, barbiturates, cannabis, cocaine, opiates, and phencyclidine (PCP). In addition, a detailed structured interview to assess duration, recency, and chronicity of use of each of these substances were conducted. Frequency of drug use was indexed using a sum score that reflected the frequency of use of various drugs including cocaine, amphetamines, heroin, and marijuana. Forty-one percent of the sample reported being drug free during the past year, and 30% endorsed using one or more of these substances once a week or more during the past year. Recent drug use was indexed on the basis of urine toxicology results. A summary score of the number of substances on which they were toxicology positive was employed as an index of recent drug use. Fifteen percent of participants were urine toxicology positive for 2 or more substances. (See Richardson, Myers, Bing, & Satz, 1997 for a detailed description of these assessment measures). All descriptive data are summarized in Table 2.

HIV serostatus was determined by enzyme-linked immunoabsorbent assay (ELISA) and confirmed by Western Blot. A serology battery was also run to assess immune function as indexed by CD4 and CD8 count and CD4/CD8 ratio.

Neuropsychological assessment was conducted using the UCLA/WHO Neuropsychology Battery (Maj et al., 1993), which is a comprehensive battery comprised of measures included in the World Health Organization's cross cultural multicenter studies of HIV-associated neuropsychiatric disorders and supplemented by traditional clinical NP tests that are widely used in the United States. The UCLA/WHO battery assesses multiple NP domains including attention, concentration, visuoconstructive abilities, psychomotor and motor speed, verbal and nonverbal memory, verbal fluency, and intellectual functioning. This battery was also supplemented with computerized measures of reaction time. Several of the domains assessed by this battery have been found to be preferentially affected by HIV infection and cocaine use. The specific measures included: Color Trails 1 & 2 (D'Elia, Satz, & Uchiyama, 1994), Color Figure Mazes 1–2–3 (D'Elia, & Satz, 1989), the Block Design and Digit Symbol subtests of the Escala de Inteligencia Wechsler para Adultos (EIWA) (Wechsler, Green, & Martinez, 1968), Grooved Pegboard Test (Matthews & Klove, 1964), Trail Making Test Parts A & B (Reitan & Wolfson, 1985), the WHO-UCLA Auditory Verbal Learning Test (Satz, Chervinsky, & D'Elia, 1993), the WHO-UCLA Picture Memory and Interference Test (Satz & Chervinsky, 1993), Verbal Fluency – Names & Animals (Benton & Hamsher, 1977), and the California Computerized Assessment Package (CalCAP) (Miller, 1991), which provides measures of simple, choice and sequential reaction times.

For purposes of analyses, tests were grouped by functional domain, and groupings were confirmed empirically by confirmatory factor analysis as described by Durvasula et al. (2000). Seven stable, reliable and interpretable NP domains were identified as follows: Verbal Memory (comprised of total words learned on the WHO-AVLT trials 1–5, WHO-AVLT short delay recall (number of words correctly recalled), WHO-AVLT long delay recall (number of words correctly recalled), and WHO-AVLT long delay recognition (number of words correctly recalled), Psychomotor Speed I (Trail Making Test Parts A & B, Color Trails 1 and 2); Psychomotor Speed II (the Block Design and Digit Symbol subtests of the EIWA and the Color Figure Maze Test, reaction time (CalCAP choice reaction time, sequential reaction time I, and sequential reaction time II, nonverbal memory (Picture Memory Test), motor speed (Grooved Pegboard), and verbal fluency.

Data Analyses

The following cofactors, known to impact neuropsychological performance in other studies of HIV, were entered as covariates in all MANCOVA analyses in order to control for other factors that could confound the effects of serostatus on NP performance: age (in years), education (in years), substance use (indexed as frequency/pattern of use of amphetamine, cocaine, heroin, and marijuana), recent drug exposure (cocaine toxicology—positive vs. negative; and marijuana toxicology—positive vs. negative) (toxicology results for only these 2 substances were entered, because less than 3% of the sample was toxicology positive for any other substance) and history of head injury/loss of consciousness (this was represented as a trichotomized score representing (a) no history of head injury; (b) history of head injury with no loss of consciousness, and (c) history of head injury with loss of consciousness.

Pair-wise comparisons were conducted to disaggregate interactive effects, and there were 16 comparisons conducted (alcohol groups by serostatus) – ((1) nondrinker – heavy drinker; (2) nondrinker – moderate drinker; (3) nondrinker – light drinker; (4) light drinker – heavy drinker; (5) light drinker – moderate drinker; (6) heavy drinker – moderate drinker), and 4 HIV comparisons within each of the alcohol groups). For the post-hocs a corrected alpha of $.05/16 = .003$ was employed to mitigate experimentwise error.

Results

Descriptive Data

Results of comparisons between alcohol use groups found significant differences on selected variables. Nondrinkers were younger than drinkers ($F(3, 489) = 2.9; p = .04$); and light drinkers evidenced the highest education levels ($F(3, 485) = 6.8; p < .001$). Differences on drug use were also observed, with significantly more moderate and heavy drinkers reporting current drug use ($\chi^2(9) = 118.1, p < .001$) compared to light and nondrinkers. In addition, a greater proportion of moderate and heavy drinkers tested positive for cocaine ($\chi^2(3) = 23.7, p < .001$) and marijuana ($\chi^2(3) = 13.1, p = .004$) than nondrinkers and light drinkers.

Thirty-eight percent of the sample reported a history of head injury. HIV negative subjects were more likely to have a history of head injury (56%) than HIV positives (47%) ($\chi^2(1) = 3.9, p = .05$). However, there was no difference between the HIV groups on history of loss of consciousness. Not surprisingly, heavy drinkers were more likely than the other alcohol use groups to report a history of head injury (68% vs. approximately 50% of the other alcohol use groups) ($\chi^2(3) = 9.1, p = .03$), and history of loss of consciousness secondary to head injury (41% vs. 21–27% of the other alcohol use groups) ($\chi^2(3) = 10.6, p = .01$). However, history of head injury or loss of consciousness was not found to be associated with performance on any of the NP testing.

Among the HIV+ sample, mean CD4 count was 724.33 ($SD = 395.2$), and no significant differences across the 4 alcohol groups on CD4 count were observed ($F(3,472) = 2.4, p = .07$).

HIV negative participants were more likely to report no lifetime drug use than the HIV positives ($\chi^2(3) = 15.2, p = .002$).

NP Performance

Psychomotor Speed—Results of the MANCOVA revealed a significant serostatus X alcohol use interaction for measures comprising the Psychomotor Speed I (Trail Making Test and Color Trails Test) domain (Wilk's $\lambda = .948, F(12, 1167) = 2.0, p = .02$), with significant univariate interactions obtained for Color Trails I ($F(3, 444) = 3.7, p = .01$), and Color Trails II ($F(3, 444) = 4.0, p = .008$). Interactions are depicted graphically for Color Trails I and II in Figures 1 and 2 respectively.

Post-hoc pairwise comparisons reveal that among the seropositives, heavy drinkers were significantly slower on Color Trails I ($t(110) = -3.00, p = .003$) and Color Trails II than light drinkers ($t(110) = -3.10, p = .002$). Among the seronegatives, moderate drinkers were significantly slower on Color Trails II than nondrinkers ($t(146) = -3.80, p < .001$) and than light drinkers ($t(160) = -3.85, p < .001$).

Reaction Time—On measures of reaction time, a significant main effect was obtained for serostatus (Wilk's $\lambda = .98, F(3, 451) = 3.4, p = .02$). A significant interaction between alcohol use and serostatus (Wilk's $\lambda = .96, F(9, 1098) = 2.2, p = .02$) (see Figures 3–5 for graphical depiction of findings) was also obtained. A significant serostatus effect was obtained for both choice reaction time ($F(1, 453) = 4.0, p = .05$), and sequential reaction time I ($F(1, 453) = 9.7, p = .002$), with SNs evidencing faster RT than SPs.

However, these alcohol effects were moderated by serostatus as evidenced by significant univariate interactions on Choice RT ($F(3, 453) = 3.4, p = .02$), Sequential RT I ($F(3, 453) = 4.1, p = .007$), and Sequential RT II ($F(3, 453) = 3.4, p = .02$).

Planned post-hoc pairwise comparisons (Bonferroni corrected) revealed that for all RT tasks seropositive heavy drinkers were significantly slower than seronegative heavy drinkers (Choice RT $t(76) = -3.40, p = .001$; Sequential RT I ($t(76) = -3.64, p = .001$; Sequential RT II ($t(76) = -3.10, p = .003$). Among seropositives, heavy drinkers were also significantly slower than moderate drinkers for both Sequential RT I ($t(53) = -3.53, p = .001$) and Sequential RT II ($t(53) = -4.02, p < .001$).

Motor Speed—On the Grooved Pegboard test, a significant interaction was found between alcohol use and serostatus (Wilk's $\lambda = .97, F(6, 922) = 2.3, p = .03$), with a significant univariate effect obtained for pegboard – nondominant hand ($F(3, 462) = 3.9; p = .009$). Results are depicted graphically in Figure 6. Examination of post-hoc comparisons revealed that among seronegatives, moderate drinkers were significantly slower than light drinkers ($t(163) = -3.04, p = .003$).

No significant main effects or interactions were obtained for measures of verbal or nonverbal memory, verbal fluency, or other psychomotor measures (measures of speeded visuconstruction, digit symbol, and the Color Figure Mazes test).

Discussion

The hypothesis that alcohol and HIV would exert an interactive effect on NP performance was upheld in the current investigation. Specifically, the findings supported the original hypotheses of a significant interaction between HIV status and alcohol consumption. Decrements in neurocognitive performance were found in HIV+ heavy drinkers and were more pronounced in domains preferentially affected by both HIV and alcohol use, specifically, psychomotor/ motor speed and reaction time. Compared to other seropositives and to seronegative heavy drinkers, HIV seropositive heavy drinkers showed the slowest performance on these measures. Consistent with previous studies, the current investigation also demonstrated that HIV seropositive participants performed more poorly than seronegatives on measures of reaction time. However, no main effects for alcohol were obtained.

On two measures of psychomotor speed — Color Trails 1 and Color Trails 2 — seropositive heavy drinkers also performed more poorly than light drinkers, and among SNs moderate drinkers were slower than nondrinkers. On a measure of motor speed (Grooved Pegboard), SN moderate drinkers were slower than light drinkers. These findings are notable as no main effects were obtained for these domains. In general, in this sample serostatus differences were noted only among the heavy drinkers — suggesting the exacerbation of cognitive deficits when persons are co-morbid for HIV and alcohol use. The interaction between HIV status and alcohol use on measures of reaction time further suggests an exacerbation of the HIV-associated deficits in information processing in HIV+ heavy drinkers, who evidenced slower reaction times than nearly all seropositive groups. Examination of the figural depictions of the findings consistently reveal SP heavy drinkers to be performing more poorly than all other groups. The results of this study are consistent with previous reports of alcohol-related (Oscar-Berman et al., 1997; Parsons & Nixon, 1993; Rourke & Loberg, 1996; Wilkinson & Poulos, 1987) and HIV-associated (Evans & Mason, 2002; Grant et al., 1987; Heaton et al., 1995; Hinkin, van Gorp, & Satz, 1995) neurocognitive deficits. In addition, the current investigation provides evidence that HIV infection and heavy alcohol use interact to exacerbate neurocognitive dysfunction.

No main effects or interactions were noted for any of the memory measures. As reported previously, studies have shown that persons diagnosed with alcohol abuse/dependence and those with long periods of alcohol use show impairment on measures of learning and memory (Bondi et al., 1998; Wilkinson & Poulos, 1987). Our failure to find an alcohol effect on measures of memory may be due to the amount of alcohol consumed in those individuals classified as “moderate” and “heavy” drinkers. Those classified as “heavy” drinkers in this study may not have met criteria as alcohol dependent in contrast to those in studies that found evidence of memory impairment. In addition, the lack of significant findings on tests of nonverbal memory may also be in part because this measure (Picture Memory Interference Test) has not been validated or empirically tested with HIV+ individuals, and as such, its utility in detecting HIV related memory deficits is unknown.

Examination of the pattern of results reveals that HIV+ moderate drinkers tended to perform better than HIV+ nondrinkers and light drinkers while among the seronegatives, moderate drinkers performed more poorly than all other alcohol groups (however, these findings did not reach statistical significance). It is possible that alcohol groups differed in their pattern of use between serostatus groups, and that seronegative moderate drinkers in our study were more likely to have more episodes of binge drinking, which may be more damaging to the CNS. Thus, heavy drinkers may drink more overall, but demonstrate a more *stable* drinking pattern with fewer episodes of binge drinking. It is also possible that although we controlled for frequency and pattern of drug use (% using drugs more than once per week), the actual *amount* of drugs used by the SN moderate drinkers was more than that used by heavy drinkers.

Moderate drinkers might also be more prone to use alcohol to “come down” after a drug binge than heavy drinkers. Therefore, the poorer performance of moderate drinkers relative to other groups might be due to differences in both pattern and amount of alcohol and drug use between these groups. The slightly better performance by moderate drinking seropositives may be an artifact of our alcohol measurement and lack of historical data. The seropositive moderate drinkers may represent a healthier subset of the sample and as such have not engaged in major changes in behaviors such as alcohol consumption in response to health concerns. Green et al. (2004) noted that, contrary to expectations, persons with histories of alcohol abuse reported less current consumption than those without such histories, and they attributed this to the possibility that people with abuse histories may have made lifestyle changes. It is possible that in our study this was true as well and the nondrinkers/light drinkers represent persons who are abstinent or more controlled in drinking patterns following treatment. These hypotheses cannot be specifically tested with the current data and should be considered in future studies. However, subsequent analyses revealed that there were no demographic differences between moderate and heavy drinkers and there were no differences between the groups with respect to progression of HIV (as determined by the proportion of individuals in each group that met diagnostic criterion for AIDS).

A recent study by Green et al. (2004) which examined the independent and interactive effects of alcohol abuse/dependence, HIV and neuropsychological performance in a small sample of HIV+ men obtained findings that are in part consistent with those obtained in this study. They found an interactive effect of alcohol abuse and HIV on executive functioning, verbal IQ and reaction time, and concluded that alcohol abuse and HIV can work synergistically to augment NP impairment. Their data in many ways deviates from ours (much smaller sample, not focused on minority men, more stringent exclusion criteria on the basis of head injury, the use of diagnostic alcohol abuse criteria), and yet the pattern of findings was generally similar. This highlights the likelihood that history of past, recent, and current alcohol consumption and abuse represent risk factors for cognitive impairment in HIV infected adults.

Our results are somewhat consistent with metabolic and electrophysiological findings of an additive effect of alcohol abuse and HIV infection (Fein et al., 1995; Fein et al., 1998; Meyerhoff et al., 1995) and suggest a common neuropathological substrate for alcohol use and HIV infection, most likely frontal brain regions. Studies have found that alcoholics show significant reductions in cerebral blood flow in frontal regions and that these reductions are associated with poorer neuropsychological functioning (Oscar-Berman & Hutner, 1993). Electrophysiological studies have also shown differences between alcoholic and non-alcoholic individuals over frontal areas (Zhang, Begleiter, & Porjesz, 1997). It is also well-documented that HIV has an affinity for the frontal-subcortical neuronal pathway (Brew et al., 1988; Navia et al., 1986).

Immune suppression represents another possible mechanism for the additive effects of HIV infection. Bagasra et al. (1990) argued that alcohol abuse may lead to increased systemic immune dysfunction in HIV seropositive individuals, which is consistent with findings of similar immunological deficits in alcoholics and those infected with HIV (Gentry, 1998). A recent study found that even when controlling for adherence to HAART, HIV+ individuals with a history of alcohol use problems have lower CD4 and higher HIV RNA levels than nondrinkers (Traphagen, Freedberg, Horton, Tripp, & Samet, 2001). This may be due to faster disease progression in alcohol users and abusers, poorer therapeutic efficacy of HAART in alcohol users and abusers, or some combination of these two mechanisms. However, a relationship between alcohol use and faster disease progression is not supported in these data, as cross sectional comparison of CD4 levels across the alcohol groups reveal no differences. It is also possible that heavy alcohol use decreases an individual's cognitive reserve, resulting in more deleterious neurocognitive deficits in HIV-infected alcohol users and abusers. Satz et

al. (1993) and Stern, Silva, Chaisson, & Evans, (1996) have noted that HIV seropositive participants with low cognitive reserve perform worse on neuropsychological measures than HIV seronegative participants and HIV seropositive participants with high cognitive reserve, suggesting that low cognitive reserve puts individuals at risk for cognitive dysfunction.

The present findings may serve as a heuristic for ongoing assessment of this issue. The AAHP was a community sample of African American men, and as such provided an externally valid representation of the HIV epidemic in Los Angeles. However, the sample was recruited as part of a study of cocaine use, and as such, many participants had a long standing history of drug use and abuse. Ninety percent of this sample reported using drugs at least once during the past year, and the comorbidity of drug and alcohol use in this sample calls for caution in interpreting findings from this study. While drug use and recent drug exposure were covaried when appropriate, it is still possible that some of the effects being observed are due in part to drug use. In this sample, moderate and heavy drinkers were more likely than other groups to report current drug use and to have used cocaine within the past 72 hours. Past work using a subset of participants from this sample has revealed little effect of cocaine use on NP functioning, and no interactive effect of cocaine use and HIV on NP functioning (Durvasula et al., 2000). Exploratory analyses revealed no relationship between self-report of marijuana use or recent exposure to marijuana as indexed by urine toxicology and NP performance. Less than 4% of the sample reported use of any substances other than cocaine or marijuana during the past year. Given past findings indicating little effect of drug use on NP functioning in this sample, these results are suggestive of an independent additive relationship between HIV and alcohol. Methodologically, it would be problematic to select a sample of HIV+ individuals who have histories of alcohol use without any drug abuse, and the uniqueness of such a sample may limit generalizability. However, our inability to definitively tease out the role of alcohol independent of drugs requires circumspection in interpretation of these findings. It is very possible that the alcohol-NP relationship observed in this sample may represent a cumulative effect of long-term drug AND alcohol use of which alcohol use may serve as a marker.

In addition, this study did not exclude participants who had a history of head injury or associated loss of consciousness. Again, to do so, would be to limit the generalizability of the sample. History of head injury secondary to impairments or accidents engendered by substance or alcohol use is not uncommon, and to exclude all persons with head injury/LOC history could result in a sample with limited ecological validity. In this sample, history of head injury or LOC was not associated with neuropsychological performance. The heavy alcohol use group did have a greater frequency of head injury and LOC history, and we recognize that a history of head injury may potentiate the effects of alcohol use and HIV, and we attempted to address this statistically by including head injury and LOC as a covariate.

The UCLA-WHO Neuropsychological test battery was employed in this study as it was believed to be more “culture-fair” and was comprised of traditional and newly developed tests that minimize the use of letters and numbers in favor of more universal stimuli such as shapes, colors, and pictorial and verbal representations of universal objects (e.g., body parts). While this battery has been shown to be useful in cross cultural settings to differentiate between HIV positive and negative participants in study sites as diverse as Germany and Zaire (Maj et al., 1993), several of the measures have not been widely used in HIV research (e.g., Color Figure Mazes, Picture Memory Interference Test), and their utility in capturing HIV related cognitive deficits is not well established. In addition, while this sample was comprised of a sample of minority men, they were all literate, and the average level of education in this sample was 13 years. This may in part explain the presence of significant findings on the Color Trails Test without finding similar results for the Trail Making Test. While the Trail Making Test requires sequencing digits and dividing between letters and numbers — both likely to be overlearned stimuli for this sample — the Color Trails Test requires attending to both numerical sequence

and color (which may be a relatively underused stimulus set for this group of participants). This is analogous to the loss of performance time typically observed on the color naming trial of the Stroop Color Word Interference Test relative to the word reading trial in literate children, adolescents, and adults. It is possible that Color Trails — although suggested to be a more “culture fair test” — may have actually challenged our participants more than the traditional Trail Making Test given the underlearned nature of the stimuli.

The present study also relied on amount of consumption to index alcohol use, and our measurement was limited to one year. As such, our conclusions reflect the impact of recent alcohol use, and do not permit generalizations about lifetime or longer term patterns of use. Bornstein et al. (1993) actually found no associations between NP impairment and alcohol abuse/dependence in asymptomatic seropositives, though they did find that quantitative estimates of alcohol use in the past year were associated with executive functioning, attention, and motor speed. Many other studies of alcohol use and neuropsychological performance have examined samples of participants with diagnoses of alcohol abuse/dependence. As this study was not originally developed as a study of alcohol abuse/dependence, this was not assessed. In addition, we did not capture drinking patterns such as binge drinking. It is possible that moderate and heavy drinkers who were binge drinkers may have had different NP outcomes than those who drank the same number of drinks per week but fewer in any one sitting.

Overall, this suggests the need for multimodal measurements of alcohol use (diagnostic criteria, amount, toxicology/recent exposure, lifetime drinking patterns) to more precisely address this issue. While it is likely that a subset of the heavy and moderate drinkers in this study would have met diagnostic criteria for alcohol abuse or dependence, the majority likely did not. It is likely that if a sample of HIV+ individuals with a history of current or past alcohol abuse/dependence were assessed, these findings may be even more pronounced.

These data were gathered in the early-mid-1990s, prior to the advent of HAART. As such, these findings may not be as applicable to current cohorts of HIV infected persons. In addition, these findings may represent a more liberal test of our hypothesis, as HAART has been found to mitigate HIV related NP decline (Deutsch et al., 2001). However, not all HIV positive individuals are receiving HAART, and many who do are nonadherent, which may result in therapeutic failure, and a diminished likelihood of CNS protection. Thus, while these data do not account for the impact of HAART on the relationship between HIV, alcohol and NP function, they do allow for description of the possible potentiation of NP decline in HIV as a function of alcohol use. Further work examining this question in current HIV infected cohorts receiving HAART is needed to empirically assess the impact of HAART in HIV+ alcohol abusers.

To our knowledge, this is the first study to examine the additive versus interactive effects of HIV and alcohol use on neurocognitive functioning in a community resident sample of African American men. The findings of the present investigation are important given the prevalence of alcohol use and abuse among individuals with HIV/AIDS and the current need to identify the problems associated with alcohol use in those with HIV/AIDS. Future studies should focus on the association between neuropsychological test performance and electrophysiological/metabolic measures of CNS functioning in seropositive alcohol users and abusers, with a close examination of activity and perfusion patterns in frontal and subcortical regions. In addition, the examination of differences in the *progression* of HIV disease in alcoholics versus non-alcoholics would provide valuable information, particularly as it relates to the treatment of alcohol users/abusers infected with HIV. It would also be important to examine the effect that periods of abstinence have on neurocognitive functioning. Studies have consistently found that length of abstinence corresponds with neuropsychological performance and that there is recovery of function with periods of abstinence (Brandt, Butters, Ryan, & Bayog 1983; Grant

et al., 1987). Future longitudinal studies could compare improvements in neurocognitive functioning in seropositive versus seronegative alcohol abusers after periods of abstinence. This study found computerized measures to be most sensitive to serostatus effects, alcohol effects, and the additive effects of the two. This highlights the importance of continuing to employ more sensitive computerized measures to capture the subtle deficits that result from HIV infection and alcohol use. Follow up studies should examine the practical implications of neurocognitive dysfunction in HIV+ alcohol users/abusers. Some investigations have suggested that alcohol and drug use are associated with nonadherence to HAART (Hinkin et al., 2002; Lin, Sethi, Wu, Strathdee, Celentano, & Vlahov, 2002; Sullivan & Nakamura, 2002), while others have noted that neurocognition is related to nonadherence to HIV medication (Durvasula, Golin, & Miller, 1999; Hinkin et al., 2001). Thus, it is possible that alcohol and HIV may also interact to negatively impact other important health behaviors such as HAART adherence.

In summary, the findings of the present study examining a large community sample of African American men are consistent with previous studies. The most notable finding, however, was the demonstration of an interactive effect of HIV status and alcohol consumption on neurocognitive functioning such that HIV+ individuals with patterns of heavy alcohol use demonstrated the worst performance relative to other seropositives as well as compared to seronegative heavy drinkers, particularly on measures of reaction time and psychomotor speed.

This study also highlights the importance of addressing the heterogeneity of HIV+ populations in NP studies. While serostatus effects were not consistently obtained, when the subset of heavy drinkers was examined, significant decrements were noted. Identification of characteristics that may compromise NP functioning such as alcohol use, drug use, history of head injury, premorbid IQ, and even low SES must be addressed to more precisely elucidate the NP sequelae of HIV infection. Neuropsychological investigations with HIV infected populations remain a methodologically challenging endeavor and results require cautious interpretation. HIV infected individuals in general appear to carry more “risky” histories (e.g., characterized by greater likelihood of drug use, neurological trauma, economic difficulties), and it is never possible to adequately “control” for all of these co-factors. As such, these results are not meant to suggest a singular explanatory role for alcohol but raise the likelihood that alcohol use, particularly heavy use, may serve as a potential marker, if not causative agent, for potentially more severe neuropsychological compromise in HIV infected individuals. Despite these limitations, the findings of this study suggest that HIV+ individuals with heavy alcohol use are at risk for neurocognitive dysfunction.

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Figure 1.
Color Trails 1.

Figure 2.
Color Trails 2.

Figure 3.
CalCAP Choice RT.

Figure 4.
CalCAP Sequential RT I.

Figure 5.
CalCAP Sequential RT II.

Figure 6.
Grooved Pegboard (Non-dominant hand).

Table 1

Sample composition by HIV serostatus and alcohol use (N = 497)

	Non drinker	Light drinker (<7 drinks/week)	Moderate drinker (7–21 drinks/week)	Heavy drinker (>21 drinks/week)
HIV negative	96 (19.3 %)	112 (22.5 %)	53 (10.7 %)	49 (9.9 %)
HIV positive	48 (9.7 %)	81 (16.3 %)	27 (5.4 %)	31 (6.2 %)
	144 (29 %)	193 (38.8 %)	80 (16.1 %)	80 (16.1 %)
				497 (100 %)

Table 2

Descriptive data

Variable	Non drinker		Light drinker		Moderate drinker		Heavy drinker		Group differences
	HIV–	HIV+	HIV–	HIV+	HIV–	HIV+	HIV–	HIV+	
Age ^a	31.9 (8.7)	34.5 (5.9)	33.5 (8.3)	35.4 (6.9)	36.4 (7.3)	34.4 (6.2)	35.5 (7.0)	36.8 (5.9)	Alcohol [*]
Education ^a	13.5 (1.9)	13.7 (2.1)	14.6 (2.4)	13.7 (2.1)	13.3 (2.0)	13.4 (1.8)	13.0 (1.9)	12.9 (2.2)	Alcohol ^{****}
Drug use ^b	14.6 %	18.8 %	16.1 %	29.6 %	43.4 %	40.7 %	61.2 %	51.6 %	Alcohol ^{****} HIV ^{**}
Cocaine Toxicology ^c	7.5 %	13.0 %	11.8 %	26.6 %	40.4 %	12.5 %	29.8 %	26.6 %	Alcohol ^{****}
Marijuana Toxicology ^c	9.6 %	8.7 %	11.8 %	16.5 %	19.6 %	20.8 %	23.4 %	30.0 %	Alcohol ^{**}
History of head injury	37.1 %	16.1 %	30.9 %	17.3 %	36.4 %	13.0 %	40.8 %	26.3 %	HIV [*] Alcohol [*]
History of LOC	16.6 %	9.4 %	12.5 %	8.9 %	17.7 %	8.9 %	23.1 %	16.7 %	Alcohol [*]
CD4 count	723.9 (383.8)		672.4 (383.1)		769.8 (427.5)		803.3 (398.1)		

*
p < .05.**
p < .01.***
p < .001.^aIn years.^b% using marijuana, amphetamines, or cocaine more than once per week during the past year.^c% toxicology positive.

Table 3

Mean neuropsychological performance by HIV and alcohol use

Variable	Non drinker		Light drinker		Moderate drinker		Heavy drinker		Group differences
	HIV−	HIV+	HIV−	HIV+	HIV−	HIV+	HIV−	HIV+	
Verbal Memory AVLT									
Trials 1–5	48.1 (9.2)	45.9 (9.8)	49.6 (8.4)	47.4 (7.5)	47.0 (9.5)	45.2 (8.4)	48.9 (7.8)	44.8 (8.8)	
Trial 7	9.8 (3.1)	9.4 (2.9)	10.2 (2.6)	9.6 (2.4)	9.3 (3.3)	9.3 (2.1)	10.0 (2.6)	9.3 (3.0)	
Trial 8	9.9 (3.0)	9.0 (2.7)	9.8 (3.0)	9.5 (2.7)	9.1 (3.2)	9.3 (2.4)	9.9 (2.9)	8.8 (2.6)	
Trial 9	13.9 (1.5)	13.8 (1.6)	14.0 (1.5)	13.9 (1.5)	13.8 (1.6)	14.1 (83)	14.2 (1.2)	13.6 (2.3)	
Trail Making Tests (seconds)									
Trails A	29.2 (19.8)	34.4 (20.6)	28.7 (10.3)	29.7 (10.0)	30.2 (9.8)	27.6 (12.2)	30.4 (16.3)	31.1 (11.4)	
Trails B	80.4 (37.6)	93.2 (47.8)	73.7 (37.0)	78.5 (36.9)	82.4 (33.1)	80.4 (43.4)	76.3 (36.2)	95.6 (50.4)	
Color Trails 1	37.1 (13.3)	44.1 (23.8)	36.8 (13.9)	37.4 (11.9)	44.0 (17.4)	37.1 (14.1)	37.4 (13.3)	48.4 (25.3)	HIV x Alcohol*
Color Trails 2	80.0 (26.4)	93.6 (38.5)	80.6 (25.9)	84.3 (29.8)	96.8 (30.4)	77.5 (27.4)	87.2 (28.1)	102.0 (35.7)	HIV X Alcohol**
Speeded and visuoconstructive tasks									
EIWA Digit Symbol ^a	62.2 (11.3)	58.2 (15.1)	63.4 (14.6)	60.6 (12.4)	56.1 (12.6)	60.1 (15.2)	59.7 (13.6)	55.1 (14.7)	
EIWA Block Design ^a	35.0 (7.7)	34.4 (8.6)	36.0 (7.0)	33.7 (8.5)	32.0 (7.3)	33.9 (6.7)	33.7 (7.7)	33.4 (8.5)	
CFM1 ^b	125.3 (41.6)	125.2 (41.7)	119.2 (47.0)	137.2 (53.8)	140.7 (43.5)	129.2 (49.4)	131.4 (46.0)	142.5 (46.5)	
CFM 2 ^b	275.1 (110.5)	262.8 (93.7)	270.0 (117.2)	286.6 (110.9)	327.0 (142.7)	328.2 (145.3)	274.6 (97.1)	323.1 (98.7)	
CFM 3 ^b	355.4 (123.8)	335.0 (121.1)	339.7 (134.2)	354.7 (132.4)	425.4 (162.3)	388.3 (164.4)	347.8 (111.7)	392.2 (127.2)	
Reaction time CalCAP									
Choice RT ^c	385.4 (54.2)	397.5 (66.3)	395.8 (63.1)	404.4 (69.8)	409.4 (58.7)	391.0 (51.2)	393.5 (54.8)	445.1 (80.9)	HIV* HIV X Alcohol*
Sequential RT I ^c	515.3 (102.1)	570.7 (112.8)	520.1 (112.1)	566.7 (102.1)	566.0 (108.7)	524.0 (114.2)	545.9 (93.9)	629.5 (113.0)	HIV** HIV X Alcohol**
Sequential RT II ^c	623.8 (129.2)	645.8 (124.9)	618.5 (131.4)	662.7 (120.8)	663.3 (117.6)	602.0 (110.6)	631.3 (118.2)	710.0 (94.5)	HIV X Alcohol*
Picture memory interference test ^d									
Book A	18.4 (1.8)	18.0 (1.9)	18.4 (1.7)	18.3 (1.9)	18.0 (2.4)	18.8 (1.4)	18.3 (2.1)	18.1 (2.1)	
Book B	15.2 (3.0)	14.4 (3.9)	14.8 (3.1)	15.3 (3.3)	14.4 (3.5)	15.5 (2.5)	15.9 (2.8)	15.4 (2.7)	
Book C	15.3 (3.7)	15.8 (3.1)	15.7 (3.1)	15.4 (3.3)	14.7 (4.1)	15.4 (3.7)	16.2 (2.6)	14.6 (3.7)	
Book D	7.4 (2.3)	7.3 (1.9)	7.7 (2.4)	7.8 (2.4)	7.6 (2.3)	7.1 (1.4)	7.6 (2.6)	7.2 (2.1)	

Variable	Non drinker		Light drinker		Moderate drinker		Heavy drinker		Group differences
	HIV−	HIV+	HIV−	HIV+	HIV−	HIV+	HIV−	HIV+	
Grooved pegboard ^b									
Dominant hand	69.7 (10.9)	73.0 (19.4)	65.7 (11.0)	68.8 (12.3)	71.3 (14.5)	71.78 (22.1)	69.2 (11.4)	74.0 (16.9)	
Nondominant hand	73.3 (13.1)	83.2 (25.8)	73.6 (13.1)	77.2 (15.8)	83.0 (28.1)	74.8 (11.1)	74.3 (18.7)	86.3 (24.5)	HIV X Alcohol *
Verbal fluency ^e									
Animals	22.5 (7.9)	21.6 (9.2)	21.9 (7.2)	20.6 (5.1)	19.4 (5.2)	20.3 (5.2)	20.5 (4.9)	20.0 (6.1)	
Names	25.9 (5.9)	24.4 (6.2)	25.9 (6.5)	26.6 (7.6)	23.5 (5.1)	24.8 (7.5)	24.5 (5.8)	24.3 (5.2)	

* p < .05.

** p < .01.

*** p < .001.

^aaw score.

^bIn seconds.

^cIn milliseconds.

^dumber of correct recognitions.

^eNumber of words.